

## CLAIMS

### What is claimed is:

1. A molecular sensing apparatus comprising:  
a first electrode;  
a second electrode;  
an insulator between said first and said second electrode; and  
a biological macromolecule connecting said first electrode to said second electrode.
2. The apparatus of claim 1, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin and a lipid.
3. The apparatus of claim 2, wherein said biological macromolecule is a nucleic acid.
4. The apparatus of claim 2, wherein said biological macromolecule is functionalized with a chemical group selected from a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, a group activatable by an electric potential.
5. The apparatus of claim 1, wherein said insulator has a resistivity greater than  $10^{-3}$  ohm-meters.
6. The apparatus of claim 5, wherein said insulator is selected from the group consisting of  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZrO}_2$ , quartz, porcelain, ceramic, polystyrene, teflon, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.
7. The apparatus of claim 1, wherein said first electrode and said second electrode are separated by a distance in the range of 1 to  $10^{10}$  Angstroms.

8. The apparatus of claim 1, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

9. The apparatus of claim 1, wherein at said first electrode and said second electrode has a resistivity of less than  $10^{-2}$  ohm-meters.

10. The apparatus of claim 1, wherein at said first electrode and said second electrode has a resistivity of less than  $10^{-3}$  ohm-meters.

11. The apparatus of claim 9, wherein the electrodes comprise a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

12. The apparatus of claim 1, wherein said first electrode is functionalized to contain a chemical group that can be derivatized or crosslinked.

13. The apparatus of claim 12, wherein the said chemical group is selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

14. The apparatus of claim 1, wherein said first electrode bears a self-assembled monolayer (SAM).

15. The apparatus of claim 14, wherein said SAM comprises a compound selected from the group consisting of an alkanethiol, a phospholipid, a bola amphiphile, and an oligo(phenylenevinylene).

16. The apparatus of claim 16, wherein the biological macromolecule is attached to the first electrode by a thiol group.

17. The apparatus of claim 16, wherein the biological macromolecule is attached to the first electrode by a phosphonate.

18. The apparatus of claim 1, wherein said biological macromolecule is attached to said first electrode by a linker.

19. The apparatus of claim 18, wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

20. The apparatus of claim 1, further comprising a substrate to support the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.

21. The apparatus of claim 1, further comprising a substrate with the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

22. The apparatus of claim 1, wherein said first electrode comprises a surface with a shape selected from the group consisting of convex, concave, textured, corrugated, patterned uniformly, and randomly patterned.

23. The apparatus of claim 1, wherein said first electrode and said second electrode are oriented in a formation selected from the group consisting of annular, planar, and orthogonal.

24. The apparatus of claim 1, wherein the first electrode comprises a first surface and a second electrode comprises a second surface wherein the first surface and the second surface are not co-planar.

25. The apparatus of claim 1, wherein the first electrode and the second electrode comprise a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second second electrode.

26. The apparatus of claim 25, wherein said apparatus comprises at least 20 electrode pairs.
27. The apparatus of claim 25, wherein said apparatus comprises at least 100 electrode pairs.
28. The apparatus of claim 25, wherein said apparatus comprises about  $10^2$  to  $10^{10}$  electrode pairs.
29. The apparatus of claim 25, further comprising a measurement device electrically coupled to the first electrode and to the second electrode of at least one electrode pair.
30. The apparatus of claim 29, wherein said measurement device measures an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.
31. The apparatus of claim 1, further comprising an electrical circuit electrically coupled to the first electrode and the second electrode.
32. The apparatus of claim 31, wherein said electrical circuit comprises an electrical signal gating system.
33. The apparatus of claim 32, wherein the said gating system comprises a CMOS gating system.
34. The apparatus of claim 25, wherein the electrodes comprising the first and second electrode pairs have attached the same biological macromolecule.
35. The apparatus of claim 25, wherein the electrodes comprising the electrode pairs have attached different biological molecules.

36. The apparatus of claim 1, further comprising a computer electrically coupled to the first electrode and the second electrode of at least one electrode pair.

37. The apparatus of claim 1, wherein at least one of the first electrode and the second electrode comprises a semi-conducting material.

38. The apparatus of claim 37, wherein said semi-conducting material has a resistivity ranging from about  $10^{-6}$   $\Omega$ -m to about  $10^7$   $\Omega$ -m.

39. The apparatus of claim 37, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,  $\text{Fe}_3\text{O}_4$ , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

40. The apparatus of claim 1, wherein said apparatus comprises:  
a first electrode having a first surface;  
a second electrode having a second surface coplanar to the first surface;  
an insulator between said first surface and said second surface; and  
a nucleic acid joining said first electrode to said second electrode.

41. A method of making a molecular sensing apparatus, said method comprising:  
providing a first electrode and a second electrode separated by an insulator;  
contacting said first and said second electrode with a first solution comprising a biological macromolecule;  
placing a charge on said first electrode to attract said biological macromolecule to said first electrode where said macromolecule attaches to said first electrode to form an attached macromolecule; and

placing a charge on said second electrode to attract a portion of said attached macromolecule to said second electrode where said macromolecule attaches to said second electrode.

42. The method of claim 41, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a proteins, a polysaccharide, a lectin, and a lipid.

43. The method of claim 41, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, a group activatable by an electric potential.

44. The method of claim 41, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin and a lipid..

45. The method of claim 41, wherein said biological macromolecule is a nucleic acid.

46. The method of claim 41, wherein said insulator has a resistivity of greater than about  $10^{-3} \Omega\text{-m}$ .

47. The method of claim 41, wherein said insulator is selected from the group containing  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZrO}_2$ , porcelain, ceramic, quartz, high resistivity plastic, and an insulating oxide or sulfide of the transition metals in the periodic table of the elements.

48. The method of claim 41, wherein said first electrode and said second electrode are separated by a distance range from about 1 to about  $10^{10}$  Angstroms.

49. The method of claim 41, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

50. The method of claim 41, wherein said first electrode and said second electrode have a resistivity of less than about  $10^{-3} \Omega\text{-m}$ .

51. The method of claim 41, wherein said first electrode and said second electrode comprise a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

52. The method of claim 41, wherein said first electrode is functionalized to bear a chemical group capable of being further derivatized or crosslinked.

53. The method of claim 52, wherein the said chemical group is selected from the group consisting of functionalized with a chemical group selected from a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, a group activatable by an electric potential.

54. The method of claim 41, wherein said biological macromolecule is attached to said first electrode by an electrically conductive linker.

55. The method of claim 54, wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

56. The method of claim 54, wherein said linker is oligo(phenylenevinylene).

57. The method of claim 41, further comprising a substrate to support the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.

58. The method of claim 41, further comprising a substrate with the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

59. The method of claim 41, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second second electrode.

60. The method of claim 59, wherein said apparatus comprises at least 3 electrode pairs.

61. The method of claim 59, wherein said apparatus comprises at least 100 electrode pairs.

62. The method of claim 59, wherein said apparatus comprises about  $10^2$  to about  $10^{10}$  electrode pairs.

63. The method of claim 59, further comprising:  
contacting said second electrode pair with a second solution comprising a second biological macromolecule;

placing a charge on a first electrode of said second electrode pair to attract said second biological macromolecule to said first electrode of said second electrode pair whereby said second biological macromolecule attaches to said first electrode to form an attached second macromolecule; and

placing a charge on said second electrode of said second electrode pair to attract a portion of said attached second macromolecule to said second electrode whereby said second macromolecule attaches to said second electrode of said second electrode pair.

64. The method of claim 63, wherein said apparatus comprises a third electrode pair.

65. The method of claim 63, wherein said apparatus comprises greater than 3 electrode pairs.



66. The method of claim 63, wherein said first solution and said second solution are the same.

67. The method of claim 63, wherein said first solution and said second solution are different.

68. The method of claim 63, wherein said first biological molecule and said second biological molecule are the same.

69. The method of claim 63, wherein said first biological molecule and said second biological molecule are the different.

70. The method of claim 41, wherein at least one of said first electrode and said second electrode comprise a semi-conducting material.

71. The method of claim 70, wherein the semi-conductor material has a resistivity in the range of  $10^{-6} \Omega\text{-m}$  to  $10^7 \Omega\text{-m}$ .

72. The method of claim 70, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,  $\text{Fe}_3\text{O}_4$ , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

73. A method of detecting an analyte, said method comprising:

- i) providing molecular sensing apparatus comprising a first electrode and a second electrode separated by an insulator where said first electrode has a biological macromolecule attached thereto;
- ii) contacting the attached macromolecule with said analyte whereby said analyte binds to said macromolecule thereby forming a macromolecule/analyte complex;
- iii) placing a charge on said second electrode attract a portion of said bound analyte to said second electrode where said analyte is bound to said second electrode

such that said macromolecule/analyte complex forms a connection between said first electrode and said second electrode; and

iv) detecting the connection between said first and said second electrode.

74. The method of claim 73, wherein said providing comprises:  
contacting said first electrode with a first solution comprising said biological macromolecule; and

placing a charge on said first electrode whereby said charge attracts said biological macromolecule to said electrode and said biological macromolecule attaches to said electrode.

75. The method of claim 73, wherein said placing a charge, further comprising placing a charge on said first electrode opposite to the charge on said second electrode.

76. The method of claim 73, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge, and magnetic potential.

77. The method of claim 73, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin, and a lipid.

78. The method of claim 77, wherein said biological macromolecule is a nucleic acid.

79. The method of claim 78, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an

alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential..

80. The method of claim 73, wherein said insulator has a resistivity greater than  $10^{-3} \Omega\text{-m}$ .

81. The method of claim 73, wherein said insulator is selected from the group consisting of  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZrO}_2$ , porcelain, ceramic, a high resistivity plastic, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.

82. The method of claim 73, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

83. The method of claim 73, wherein said first electrode and said second electrode are separated by a distance ranging from about 1 to about  $10^{10}$  Angstroms.

84. The method of claim 73, wherein said first electrode and said second electrode have a resistivity of less than about  $10^{-2} \Omega\text{-m}$ .

85. The method of claim 73, wherein said first electrode comprises a semi-conductor material.

86. The method of claim 88, wherein said semi-conductor material having a resistivity ranging from about  $10^{-6} \Omega\text{-m}$  to about  $10^7 \Omega\text{-m}$ .

87. The method of claim 88, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,  $\text{Fe}_3\text{O}_4$ , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

88. The method of claim 73, wherein said first electrode and said second electrode are formed from a material selected from the group consisting of ruthenium, osmium,

cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

89. The method of claim 73, wherein at least one said first electrode is functionalized to bear a chemical group capable of being further derivatized or crosslinked.

90. The method of claim 89, wherein the said chemical group is selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

91. The method of claim 89, wherein said functionalized biological macromolecule is attached to said first electrode by an electrically conductive linker.

92. The method of claim 91, wherein said linker is selected from the group consisting of DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

93. The method of claim 91, wherein said linker is oligo(phenylenevinylene).

94. The method of claim 73, wherein the first electrode and the second electrode are integrated with a substrate.

95. The method of claim 73, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

96. The method of claim 73, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second electrode.

97. The method of claim 96, wherein said apparatus comprises at least 3 electrode pairs.

98. The method of claim 96, wherein said apparatus comprises at least 100 electrode pairs.

99. The method of claim 96, wherein said apparatus comprises from about  $10^2$  to about  $10^{10}$  electrode pairs.

100. The method of claim 96, further comprising performing steps ii, iii, and iv with said second electrode pair.

101. The method of claim 96, wherein the biological macromolecule on said first electrode pair is different than the biological macromolecule attached to the second electrode pair.

102. A method of detecting an analyte, said method comprising:

i) providing a molecular sensing apparatus comprising a first electrode and a second electrode separated by an insulator where said first electrode has a first biological macromolecule attached thereto and said second electrode has a second biological macromolecule attached thereto;

ii) contacting the first attached macromolecule and the second attached macromolecule with said analyte whereby said analyte binds to the first macromolecule and to the second macromolecule thereby forming a macromolecule/analyte complex forming a connection between said first electrode and said second electrode; and

iii) detecting the connection between said first and said second electrode.

103. The method of claim 102, wherein said providing comprises:

contacting said first electrode with a first solution comprising said first biological macromolecule; and

placing a charge on said first electrode whereby said charge attracts said first biological macromolecule to said electrode and said biological macromolecule attaches to said electrode.

104. The method of claim 102, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permitivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

105. The method of claim 102, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin, and a lipid.

106. The method of claim 105, wherein said biological macromolecule is a nucleic acid.

107. The method of claim 106, wherein said biological macromolecule is functionalized with a chemical group selected from the group consisting of a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

108. The method of claim 102, wherein said insulator has a resistivity greater than  $10^{-3}\Omega\cdot\text{m}$ .

109. The method of claim 102, wherein said insulator is selected from the group consisting of  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZrO}_2$ , ceramic, porcelain, a high resistivity plastic, and an insulating oxide or sulfide of a transition metal in the periodic table of the elements.

110. The method of claim 102, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

111. The method of claim 102, wherein said first electrode and said second electrode are separated by a distance ranging from about 1 to about  $10^{10}$  Angstroms.

112. The method of claim 102, wherein said first electrode and said second electrode have a resistivity of less than about  $10^{-2} \Omega\text{-m}$ .

113. The method of claim 102, wherein said first electrode and said second electrode comprise a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

114. The method of claim 102, wherein at least one of the first electrode and the second electrode comprises a semi-conductor material.

115. The method of claim 114, wherein said semi-conductor material has a resistivity ranging from about  $10^{-3} \Omega\text{-cm}$  to about  $10^7 \Omega\text{-m}$ .

116. The method of claim 114, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,  $\text{Fe}_3\text{O}_4$ , germanium, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, Te, PbS, InSb, PbTe, PbSe, and tungsten disulfide.

117. The method of claim 102, wherein said first electrode and said second electrode are formed from a material selected from the group consisting of ruthenium, osmium, cobalt, rhodium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon, and a carbon nanotube.

118. The method of claim 102, wherein at least one of the said first electrode and second electrode is functionalized to contain a chemical group capable of being further derivatized or crosslinked.

119. The method of claim 118, wherein the said chemical group is selected from the group consisting of an a sulfate, a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, a bromine, an iodine, a chlorine, a light-activatable group, and a group activatable by an electric potential.

120. The method of claim 118, wherein said functionalized biological macromolecule is attached to said first electrode by an electrically conductive linker.

121. The method of claim 120, wherein said linker is selected from the group consisting DFDNB, DST, ABH, ANB-NOS, EDC, NHS-ASA, and SIA.

122. The method of claim 120, wherein said linker is oligo(phenylenevinylene).

123. The method of claim 102, wherein the first electrode and the second electrode are integrated with a substrate.

124. The method of claim 102, wherein the first electrode and the second electrode are integrated with the insulator to form a substrate.

125. The method of claim 102, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second electrode.

126. The method of claim 125, wherein said apparatus comprises at least 3 electrode pairs.

127. The method of claim 125, wherein said apparatus comprises at least 100 electrode pairs.

128. The method of claim 125, wherein said apparatus comprises from about  $10^2$  to about  $10^{10}$  electrode pairs.



129. The method of claim 125, further comprising performing steps ii and iii with said second electrode pair.

130. The method of claim 125, wherein at least one of the biological macromolecule on an electrode of the second pair is different from either of the biological macromolecules on the electrodes of the first electrode pair.

131. The method of claim 125, wherein the biological macromolecules on the electrode of the second electrode pair are different from the biological macromolecules on the electrodes of the first electrode pair.

132. A method of detecting an analyte, said method comprising:

- i) providing a molecular sensing apparatus comprising a first electrode and a second electrode separated by an insulator where a biological macromolecule forms a connection between said first electrode and said second electrode;
- ii) detecting the connection between said first and said second electrode;
- iii) contacting the attached macromolecule with said analyte whereby said analyte binds to said macromolecule forming a macromolecule/analyte complex; and
- iv) detecting the difference in the connection between said first electrode and said second electrode.

133. The method of claim 132, wherein said contacting comprises placing a charge on said first electrode whereby said charge attracts said analyte to said biological macromolecule.

134. The method of claim 132, wherein said providing comprises:  
contacting said first electrode with a first solution comprising said biological macromolecule; and  
placing a charge on said first electrode whereby said charge attracts said biological macromolecule to said electrode and said biological macromolecule attaches to said electrode.

placing a charge on said second electrode to attract a portion of said bound macromolecule to said second electrode where said macromolecule is bound to said second electrode such that said macromolecule forms a connection between said first electrode and said second electrode.

135. The method of claim 132, wherein said placing charge comprises placing a charge on said first electrode opposite to the charge on said second electrode.

136. The method of claim 132, wherein said detecting comprises detecting an electromagnetic property selected from the group consisting of direct electric current, alternating electric current, permittivity, resistivity, electron transfer, electron tunneling, electron hopping, electron transport, electron conductance, voltage, electrical impedance, signal loss, dissipation factor, resistance, capacitance, inductance, magnetic field, electrical potential, charge and magnetic potential.

137. The method of claim 132, wherein said biological macromolecule is selected from the group consisting of a nucleic acid, a protein, a polysaccharide, a lectin or a lipid.

138. The method of claim 132, wherein said biological macromolecule is a nucleic acid.

139. The method of claim 132, wherein said analyte is a protein or protein complex.

140. The method of claim 132, wherein said biological macromolecule is functionalized with a chemical group consisting of a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, a phosphonate, an alkene, an alkyne, a hydroxyl group, bromine, iodine, chlorine, a chemical group that can be activated by light, and a chemical group that can be activated by the application of an electrical potential.

141. The method of claim 132, wherein said insulator is selected from the group consisting of elements, compounds or substances that have resistivities greater than  $10^3 \Omega\text{-m}$ .

142. The method of claim 141, wherein said insulator is selected from the group containing  $\text{SiO}_2$ ,  $\text{TiO}_2$ ,  $\text{ZrO}_2$ , porcelain, polystyrene, polystyrene, organic compounds produced by polymerization having a resistivity greater than  $10^{-3} \Omega\text{-m}$  and insulating oxides or sulfides of the transition metals in the periodic table of the elements.

143. The method of claim 132, wherein said first electrode and said second electrode are separated by a distance less than about 70 Angstroms.

144. The method of claim 132, wherein said first electrode and said second electrode are separated by a distance in the range of 1 to  $10^{10}$  Angstroms.

145. The method of claim 132, wherein at least one said first electrode and said second electrode are formed of a material selected from the group consisting of elements, compounds or substances that have resistivities of less than  $10^{-2} \Omega\text{-m}$ .

146. The method of claim 145, wherein the said first electrode and said second electrode are formed from a material selected from the group consisting of, ruthenium, osmium, cobalt, rhodium, rubidium, lithium, sodium, potassium, vanadium, cesium, beryllium, magnesium, calcium, chromium, molybdenum, silicon, germanium, aluminum, iridium, nickel, palladium, platinum, iron, copper, titanium, tungsten, silver, gold, zinc, cadmium, indium tin oxide, carbon or carbon nanotubes or alloys or compounds of these materials.

147. The method of claim 132, wherein at least one of the first electrode and the second electrode comprises a semiconductor material.

148. The method of claim 132, wherein said semi-conductor material has a resistivity ranging from about  $10^{-2} \Omega\text{-m}$  to about  $10^9 \Omega\text{-m}$ .

149. The method of claim 148, wherein the semi-conducting material is selected from the group consisting of silicon, dense silicon carbide, boron carbide,  $\text{Fe}_3\text{O}_4$ , germanum, silicon germanium, silicon carbide, tungsten carbide, titanium carbide, indium phosphide, gallium nitride, gallium phosphide, aluminum phosphide, aluminum arsenide, mercury cadmium telluride, tellurium, selenium, tungsten disulfide, ZnS, ZnO, ZnSe, CdS, ZnTe, GaSe, CdSe, CdTe, GaAs, InP, GaSb, InAs, PbS, InSb, PbTe, and PbSe.

150. The method of claim 132, wherein at least one of the said first electrode and second electrode is functionalized to contain a chemical group capable of being further derivatized or crosslinked.

151. The method of claim 150, wherein the said chemical group is selected from the group consisting of a sulfhydryl, an amine, an aldehyde, a carboxylic acid, a phosphate, an alkene, an alkyne, a hydroxyl group, bromine, iodine, chlorine, a chemical group that can be activated by light of wavelength ranging from 190 nm to 700 nm, such as an aryl azide, a fluorinated aryl azide, a benzophenone, (R,S) -1-(3,4- (methylene-dioxy)-6-nitrophenyl) ethyl chloroformate – (MeNPOC), N-((2-pyridyl, ethyl)-4-azido) salicylamide or a chemical group that can be activated by the application of an electrical potential, such as S-benzyloxycarbonyl derivatives, S-benzyl thioethers, S-phenyl thioethers, S-4-picolyl thioethers, S-2,2,2-trichloroethoxycarbonyl derivatives, S-triphenylmethyl thioethers.

152. The method of claim 132, wherein said biological macromolecule is attached to said first electrode by an electrically conductive linker.

153. The method of claim 132, wherein said linker is selected from the group consisting of chemical crosslinkers capable of linking functional groups, such as DFDNB, DST, ABH, ANB-NOS, EDC, NHS, NHS-ASA, SLA.

154. The method of claim 132, wherein said linker is an oligo(phenylenevinylene).

155. The method of claim 132, wherein said apparatus further comprises substrate to support the first electrode and the second electrode, wherein the first electrode and the second electrode are integrated with the substrate.

156. The method of claim 132, wherein said apparatus further comprises a substrate in which the first electrode and the second electrode are integrated with the insulator to form the substrate.

157. The method of claim 132, wherein the first electrode and the second electrode provide a first electrode pair, the molecular sensing apparatus further comprising a second electrode pair comprising a second first electrode and a second second electrode.

158. The method of claim 157, wherein said apparatus comprises at least 3 electrode pairs.

159. The method of claim 157, wherein said apparatus comprises at least 100 electrode pairs.

160. The method of claim 157, wherein said apparatus comprises in the range of  $10^2$  to  $10^{10}$  electrode pairs.

161. The method of claim 157, further comprising performing steps ii, iii and iv with the second electrode pair.

162. The method of claim 157, wherein the biological macromolecule attached to said first electrode pair is the same as the biological macromolecule attached to said second electrode pair.

163. The method of claim 157, wherein the biological macromolecule attached to said first electrode pair is different from the biological macromolecule attached to said second electrode pair.

164. The method of claim 157, wherein the analyte attached to said first electrode pair is the same as the analyte attached to said second electrode pair.

165. The method of claim 157, wherein the analyte attached to said first electrode pair is different from the analyte attached to said second electrode pair.

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